Amendments to the Claims

Applicants amend claims 1, 8, 24, 25, 43, 51, 139, 140, 141, 145, 146, 148 and cancel claims 2, 36, 49 and 138 and add new claims 154-156. Claims 1, 6, 8-11, 24, 25, 28, 29, 43, 50, 51, 62, 65, 68, 69 and 139-156 remain pending upon entry of this amendment. Amendments to the claims are provided in the listing of claims provided below.

Listing of Claims

1. (currently amended) A device for monitoring the migration or invasion of a biological particle such as a cell, which device comprises:

a) an upper chamber adapted to receive and retain a cell sample;

b) a lower chamber comprising at least two electrodes; and,

c) a biocompatible porous membrane having a porosity sufficient to allow cells to migrate therethrough, wherein said membrane is disposed in the device so as to separate the upper and lower chambers from one another, wherein said at least two electrodes are disposed on said membrane;

wherein migration of cells through the porous membrane permits contact between the migrating cells and one or more of at least two electrodes of said lower chamber, wherein said at least two electrodes have substantially the same surface area, and further wherein ~~further~~ said contact at any one or more of said at least two electrodes provides a detectable change in impedance between or among the electrodes.

2 – 5 (canceled)

6. (original) The device according to Claim 1, further comprising an impedance analyzer in electrical communication with the at least two electrodes.

7. (canceled)

8. (currently amended) The device according to Claim 1, wherein the biocompatible porous membrane comprises ~~glass, sapphire, silicon, silicon dioxide on silicon, or~~ one or more polymers and further wherein the thickness of said membrane has a thickness ~~between~~ from 5 microns to 50 microns~~2 microns and 500 microns~~.

9. (original) The device according to Claim 1, wherein the biocompatible porous membrane further comprises a coating for promoting the attachment of one or more cells thereto.

10. (original) The device according to Claim 1, further comprising

a) electrically conductive traces extending from, and in electrical communication with, the at least two electrodes; and,

b) connection means for establishing electrical communication between the electrically conductive traces and an impedance analyzer.

11. (previously presented) A method for monitoring the migration or invasion of a cell, the method comprising:

a) providing a device according to Claim 1;

b) introducing the cells into the upper chamber of the device; and,

c) determining whether a change in impedance between or among the electrodes occurs, where a change in impedance between or among the electrodes is indicative of the invasion of, or migration of cells into or through, the biocompatible porous membrane.

12 – 23 (canceled)

24. (currently amended) A device for measuring electrical impedance, resistance, or capacitance of a cell/substrate interface, comprising two or more electrodes having substantially the same surface area fabricated on one side of a flexible biocompatible membrane that comprises at least one pore, wherein said device has a surface suitable for cell attachment or growth, further wherein cell attachment or growth results in cellular contact with at least one of said two or more electrodes further resulting in a detectable change in electrical impedance, resistance or capacitance.

25. (currently amended) The device according to Claim 24, wherein said biocompatible membrane comprises ~~glass, sapphire, silicon, silicon dioxide on silicon,~~ one or more plastics[[,]] or one or more polymers and further wherein the thickness of said membrane is from [[2]] 5 microns to 50 ~~500~~ microns.

26. (canceled)

27. (canceled)

28. (original) The device according to Claim 25, wherein said biocompatible membrane comprises a coating that allows the attachment of one or more cells.

29. (original) The device according to Claim 28, wherein said coating comprises an extracellular matrix component.

30-42 (canceled)

43. (currently amended) The device according to Claim [[36]] 24 situated in a fluid container, wherein the device separates an upper chamber from a lower chamber of the fluid container.

44 – 49 (canceled)

50. (previously presented) The device according to Claim 24, wherein said two or more electrodes comprise at least four electrodes and the at least four electrodes are arranged in an electrode structure array of two or more interdigitated electrode structure units (IDES) or concentric electrode structure units (CCES), each of which comprises at least two electrodes.

51. (currently amended) A device comprising the device of Claim 50, wherein said biocompatible membrane is reversibly or irreversibly attached to a structure that provides a plurality of isolated fluid containers such that at least one of the fluid containers comprises a single IDES or CCES structure unit, wherein for each of said plurality of isolated fluid containers that comprises a single IDES or CCES, the exposed surface area of said one side of said biocompatible membrane on which electrodes are fabricated comprises an approximately uniform distribution of electrodes or electrode elements.

52 – 61 (canceled)

62. (previously presented) The device according to Claim 43, wherein said at least two electrodes are fabricated on the lower side of said membrane, wherein said at least one pore has a diameter of between 1 micron and 30 microns.

63. (canceled)

64. (canceled)

65. (previously presented) The device according to Claim 62, wherein said membrane comprises at least one biomolecular coating, at least one extracellular matrix component, a layer of epithelial or endothelial cells, or a combination thereof, on the upper side of said membrane.

66. (canceled)

67. (canceled)

68. (previously presented) The device according to Claim 62, wherein said device is used to assay the migration or invasiveness of one or more cells and wherein said lower chamber comprises at least one compound known to modulate the migration or invasiveness of cells, or at least one compound suspected of modulating the migration or invasiveness of cells.

69. (previously presented) The device according to Claim 62, wherein said device is used to assay the migration or invasiveness of one or more cells and said upper chamber comprises at least one compound known to modulate the migration or invasiveness of cells, or at least one compound suspected of modulating the migration or invasiveness of cells.

70 – 138 (canceled)

139. (currently amended) The device according to Claim [[36]] 24 , wherein the at least two electrodes that have substantially the same surface area are in an interdigitated or a concentric configuration.

140. (currently amended) The device according to Claim [[36]] 24 , wherein the at least two electrodes have a geometry selected from the group consisting of circle-on-line, diamond-on-line, castellated, and sinusoidal geometries.

141. (currently amended) The device according to Claim [[36]] 24 , wherein the width of the electrodes is from 20 microns to 500 microns; further wherein the gap between electrode elements is between 3 microns and 80 microns in width; further wherein the ratio of the gap width to the electrode element width ranges from about 1:20 to about 3:1; further wherein the gap between electrode elements is between about 0.2 time and about 3 times the width of cells used in the measuring electrical impedance, resistance or capacitance of a cell/substrate interface.

142 (previously presented) The device of Claim 51, further comprising an impedance analyzer connected to the electrodes.

143. (previously presented) An apparatus for measuring electrical impedance, resistance, or capacitance of a cell/substrate interface, comprising a plate that comprises one or more wells, at least one of which comprises the device of Claim 24, wherein each device separates each well into upper and lower chambers.

144. (previously presented) The apparatus according to Claim 143, wherein the two or more electrodes are on the lower side of the membrane.

145. (currently amended) The apparatus according to Claim 143, wherein the two or more electrodes are on the upper side of the membrane ~~and wherein the pores of the biocompatible membrane have a diameter of less than 5 microns~~.

146. (currently amended) The apparatus according to Claim 143, ~~comprising the device of Claim 51,~~

wherein said two or more electrodes comprise at least four electrodes and the at least four electrodes are arranged in an electrode structure array of two or more interdigitated electrode structure units (IDES) or concentric electrode structure units (CCES), each of which comprises at least two electrodes,

further wherein the biocompatible membrane is reversibly or irreversibly attached to a first plate that comprises two or more wells that provide lower chambers of cell migration units and is reversibly or irreversibly attached to a second plate that provides tube structures that provide upper chambers of cell migration units, such that each cell migration unit comprises a single IDES or CCES.

147. (previously presented) The apparatus according to Claim 145, wherein said membrane comprises a layer of cells on the upper side of the membrane, wherein said cells are epithelial cells or endothelial cells.

148. (currently amended) An apparatus according to Claim 143, further comprising an insert tray that comprises one or more insert chamber, each of which comprising:

(a) fluid impermeable walls, and

(b) ~~the device of Claim 24~~wherein said device form~~s~~~~ing~~ the bottom of each of said one or more insert chamber;

further wherein each insert chamber fits into a well of said plate such that the wells of the plate form a lower chamber and the insert forms an upper chamber of a cell invasion/migration unit.

149. (previously presented) The apparatus according to Claim 146, further comprising an impedance analyzer, interface electronics comprising electronic switches to control and switch said impedance analyzer to different electrode structure units of said apparatus, and a software that can enable real time measurement or monitoring of impedance between the electrodes or electrode structures of said apparatus.

150. (previously presented) The apparatus according to Claim 149, wherein said software has at least one function selected from the group consisting of:

(a) controlling electronic switching for connecting said impedance analyzer to one of multiple electrode structure units of the present apparatuses;

(b) controlling impedance analyzer for measurement of impedance between or among electrode structures at one or multiple frequencies;

(c) processing the acquired impedance data to derive appropriate biologically relevant parameters (e.g., cell number index);

(d) displaying the results on a monitor or storing results; and

(e) automatically performing above functions (a) through (d) at regular or irregular time intervals.

151. (previously presented) A method for monitoring cell migration or invasion, comprising:

a) providing an apparatus of claim 144;

b) placing cells in the upper chamber of said apparatus ; and

c) monitoring a change of impedance between or among the electrodes to monitor migration or invasion of said cells.

152. (previously presented) The method according to Claim 151, further comprising adding a known or suspected modulator of cell migration or cell invasion to the lower chamber of said apparatus.

153. (previously presented) The method according to Claim 151, further comprising adding a known or suspected modulator of cell migration or cell invasion to the upper chamber of said apparatus.

154. (newly added) The apparatus according to claim 145, wherein said at least one pore of the biocompatible membrane has a diameter of less than 5 microns.

155. (newly added) The apparatus according to claim 145, wherein said membrane comprises a layer of cells on the upper side of said membrane, wherein said cells are Caco-2 cells.

156. (newly added) A method of measuring the integrity of a cell monolayer, comprising:

a) providing the apparatus of claim 145;

b) culturing cells in said upper chamber of said apparatus; and

c) monitoring the integrity of the cell monolayer in said upper chamber by monitoring the impedance.